

**CLAIMS:**

1. A process for sensing biological or chemical changes in molecular structural shape (or mass) of molecules attached to the surface of a transverse shear piezoelectric (oscillating molecular) sensing device driven by a network analyzer, said process comprising:
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- i) exciting said sensor device at a series of predetermined frequencies;
  - 10 ii) collecting data to determine values for the predetermined parameters of series resonance frequency shift ( $f_s$ ), motional resistance (RM), motional inductance (LM), motional capacitance (CM), electrostatic capacitance ( $C_o$ ) and boundary layer slip parameter ( $\alpha$ ); and
  - 15 iii) determining relative changes in said measured parameters to detect thereby any changes in molecular structural shape or mass at sensing device surface.
2. The process according to claim 1 further comprising the step of:
- iv) correlating said changes with a calibrated set of data for said parameters to determine a value for change in molecular conformation and/or molecular mass.
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3. The process according to claim 1 wherein a change in slip parameter ( $\alpha$ ) and an essentially zero change in series resonant frequency shift confirms a change in molecular structural shape and essentially zero change in mass.
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4. The process according to claim 1 wherein said changes in molecular mass or conformation are generated by an interaction between entities bound to the sensor and molecules in the surrounding liquid medium.
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5. The process according to claim 4 wherein said entities bound to the sensor are selected from the group consisting of proteins and nucleic acids.

6. The process according to claim 5 wherein said proteins are selected from the group consisting of antibodies, enzymes, molecular receptors, receptor ligands and polypeptides.

5 7. The process according to claim 5 wherein said nucleic acids are selected from the group consisting of DNA, RNA and oligonucleotides.

8. The process according to claim 4 wherein said molecules in liquid medium are selected from the group consisting of proteins and nucleic acids.

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9. The process according to claim 8 wherein said proteins are selected from the group consisting of antibodies, enzymes, molecular receptors, receptor ligands and polypeptides.

15 10. The process according to claim 8 wherein said nucleic acids are selected from the group consisting of DNA, RNA and oligonucleotides.

11. A method of determining the efficiency of acoustic coupling between a sensor and the surrounding fluid, said method comprising:

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a) applying an electrical signal of known frequency and voltage to the sensor;

b) measuring the current through the sensor to determine the impedance at the known frequency;

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c) repeating steps a) and b) over a range of frequencies to generate a set of impedance data; and

d) fitting the measured impedance data to determine an  $\alpha$  parameter which represents coupling strength.

12. The method according to claim 11, wherein the  $\alpha$  parameter is other than 1.

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13. The method according to claim 11 wherein the magnitude of said  $\alpha$  parameter is dependant on molecular mass and/or molecular conformation at the sensor surface.